UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,277	03/25/2002	Dexian Dou	1059.00051	3577

7590 07/26/2004

Kenneth I Kohn
Kohn & Associates
30500 Northwestern Highway Suite 410
Farmington Hills, MI 48334

EXAMINER	
LANDSMAN, ROBERT S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,277	DOU ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-4 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 3/25/02 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/23/02; 9/11/03; 8/29/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Formal Matters

A. The Preliminary Amendment dated 3/25/02 has been entered into the record.

B. Claims 1-4 are pending and are the subject of this Office Action.

C. The Information Disclosure Statement dated 9/23/02 has been entered into the record.

D. The Information Disclosure Statement dated 8/29/03 has been entered into the record.

E. The Information Disclosure Statement dated 9/11/03 has been entered into the record.

2. Oath/Declaration

A. The Oath/Declaration is missing. It appears from Applicants' statements that Applicants have provided an Oath. If this is the case, the Examiner requests that Applicants identify the date of submission.

B. Furthermore, Applicants have provided a "Statement of Facts" and a letter under 37 CFR 1.47 regarding the inventor Dr. Dou. However, no petition could be found in the file. Again, if Applicants have submitted a petition, the Examiner requests that Applicants identify the date of submission. A decision regarding Dr. Dou can only be made by the Office of Petitions.

3. Specification

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The claims are drawn toward the Kringle proteins and methods of using the protein.

B. Though none could be found, Applicant is advised that embedded hyperlinks and/or other forms of browser-executable code are impermissible and require deletion. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01(p), paragraph I regarding incorporation by reference.

C. Figure 5 is objected to since Figure 5 is not labeled as parts "A" and "B", contrary to the Brief Description.

4. Claim Rejections - 35 USC § 112, first paragraph - scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the KED of Figure 3 (though the sequence is not known) and its use in a particular cancer model and for and kringles 1-5 of Figure 6, does not reasonably provide enablement for "**pharmaceutical compositions**" comprising all kringle proteins, all kringle proteins "**derived from**" tPA or all methods of "**treating all tumors**" with kringle proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming pharmaceutical compositions comprising all kringle proteins, including those "derived from tPA" as well as methods of treating all tumors with kringle proteins. These proteins, as well as their derivatives, would have one or more amino acid substitutions, deletions, insertions and/or additions to the kringle proteins disclosed in the speicfication. Furthermore, the KED protein has not been identified by SEQ ID NO, so it is not clear as to which KED the application involves. Similarly, the scope of the invention would be limited to only that KED disclosed in the specification.

Applicants provide only minimal guidance and working examples of kringle and proteins and no guidance or working examples of "derivatives." Furthermore, Applicants have not demonstrated that kringles can be used to treat tumors in a patient, nor that all tumors can be treated by KED or kringle proteins, especially in light of the fact that solid tumors and blood-bourne tumors such as lymphomas have different characteristics. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional kringle or KED protein other than those disclosed in the specification, including those from other species. The critical residues which would be required to maintain protein function have not been disclosed in the specification.

In summary, the breadth of the claims is excessive with regard to Applicants claiming claiming pharmaceutical compositions comprising all kringle proteins, including those "derived from tPA" as well as methods of treating all tumors with kringle proteins. There is also minimal guidance and working examples of kringle and KED proteins and no working examples of derivatives or how to treat all tumors, such as blood-

bourne tumors. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a functional protein other than those disclosed in the specification leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

5. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. "KED," "Kringle 1-5," and "derivatives" thereof would encompass proteins with one or more amino acid substitutions, deletions, insertions and/or additions to the proteins disclosed in the specification.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "kringle" and "KED" alone are insufficient to describe the genus.

The specification provides a written description of only a small number of these constructs. No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical amino acid residues which would structurally characterize the genus of kringle and KED proteins claimed, because it is unknown and not described what structurally constitutes any different amino acids encoding kringle or KED proteins, or amino acids encoding kringle and KED from any different species, which are further not described, or any different amino acid sequence which is a "derivative" to the disclosed proteins; thereby not meeting the written description requirement under 35 USC 112, first paragraph. Therefore, one of skill in the art

would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

6. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 2 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "consisting essentially of." The metes and bounds of this phrase are not known.

7. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being unpatentable by Henkin et al. (US Patent No. 6,743,428). The claims recite pharmaceutical compositions comprising kringle protein and KED proteins as well as methods of treating tumors using these proteins. Henkin teach kringle proteins are that they can be used in pharmaceutical compositions to treat angiogenic disease (Abstract), which contributes to cancer and tumor growth (paragraph [0004], [0011], [0046] and [0051]). These kringle proteins would be considered "derived from" a tPA, especially in the absence of a definition of the term "derived from." Henkin teach the use of kringle 5 ([0047]). Paragraph [0027] teaches the use of kringle 5 with endostatin (KED).

8. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Fax draft or informal communications with the examiner should be directed to (571) 273-0888.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-0700.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
July 15, 2004

ROBERT LANDSMAN
PATENT EXAMINER